

Computational Chemistry- Advancements and Scope

Harshita Patodia

Abstract

Computational chemistry is a branch of chemistry that uses computer simulation to assist in solving chemical problems. It uses methods of theoretical chemistry, incorporated into efficient computer programs, to calculate the structures and properties of molecules and solids. It is necessary because, apart from relatively recent results concerning the hydrogen molecular ion (dihydrogen cation, see references therein for more details), the quantum many-body problem cannot be solved analytically, much less in closed form. While computational results normally complement the information obtained by chemical experiments, it can in some cases predict hitherto unobserved chemical phenomena. It is widely used in the design of new drugs and materials.

Examples of such properties are structure (i.e., the expected positions of the constituent atoms), absolute and relative (interaction) energies, electronic charge density distributions, dipoles and higher multipole moments, vibrational frequencies, reactivity, or other spectroscopic quantities, and cross sections for collision with other particles.

The methods used cover both static and dynamic situations. In all cases, the computer time and other resources (such as memory and disk space) increase rapidly with the size of the system being studied. That system can be one molecule, a group of molecules, or a solid. Computational chemistry methods range from very approximate to highly accurate; the latter are usually feasible for small systems only. Ab initio methods are based entirely on quantum mechanics and basic physical constants. Other methods are called empirical or semi-empirical because they use additional empirical parameters.

Both ab initio and semi-empirical approaches involve approximations. These range from simplified forms of the first-principles equations that are easier or faster to solve, to approximations limiting the size of the system (for example, periodic boundary conditions), to fundamental approximations to the underlying equations that are required to achieve any solution to them at all. For example, most ab initio calculations make the Born–Oppenheimer approximation, which greatly simplifies the underlying Schrödinger equation by assuming that the nuclei remain in place during the calculation. In principle, ab initio methods eventually converge to the exact solution of the underlying equations as the number of approximations is reduced. In practice, however, it is impossible to eliminate all approximations, and residual error inevitably remains. The goal of computational chemistry is to minimize this residual error while keeping the calculations tractable.

In some cases, the details of electronic structure are less important than the long-time phase space behavior of molecules. This is the case in conformational studies of proteins and protein-ligand binding thermodynamics. Classical approximations to the potential energy surface are used, as they are computationally less intensive than electronic calculations, to enable longer simulations of molecular dynamics. Furthermore, cheminformatics uses even more empirical (and computationally cheaper) methods like machine learning based on physicochemical properties. One typical problem in

cheminformatics is to predict the binding affinity of drug molecules to a given target.

Introduction

Computational chemists may use high-performance computing (supercomputers and computing clusters) to solve problems and create simulations that require massive amounts of data. Tools of computational chemists include electronic structure methods, molecular dynamics simulations, quantitative structure–activity relationships, cheminformatics, and full statistical analysis.

Computational chemistry is not the same as computer science, although professionals in the two fields commonly collaborate. Computer scientists devote their time to developing and validating computer algorithms, software and hardware products, and data visualization capabilities. Computational chemists work with laboratory and theoretical scientists to apply these capabilities to modeling and simulation, data analysis, and visualization to support their research efforts.(1)

Many computational chemists develop and apply computer codes and algorithms, although practicing computational chemists can have rewarding careers without working on code development. Programming skills include compiling FORTRAN or C code, performing shell scripting with bash, Tcl/Tk, python, or perl, performing statistical analysis using R or SPSS, and working within a Windows, MacOS, or Linux environment.

As cheminformatics tools and computational modeling platforms develop, it becomes easier to define workflow tasks through graphically based workbench environments. A recent trend in reduced-order modeling and similar methods is enabling fairly powerful computational tools to be implemented on portable devices, including tablets and smart phones. This enables researchers to perform what-if calculations and try out various scenarios while they are in the plant or out in the field.

Typical work duties include the following:

- Develop computer models and simulations of chemical and biochemical processes and entities
- Perform and interpret statistical analysis of large datasets
- Create visual representations of reaction pathways, molecular interactions, or other phenomena
- Collaborate with laboratory researchers in industrial, nonprofit, government, or academic laboratories
- Characterize new compounds and processes to support patent claims
- Help develop synthesis processes by identifying and characterizing reaction pathways and identifying the most likely products
- Apply new software and hardware capabilities for data collection and analysis
- Provide customer support as an employee of a service laboratory or a sales or service representative of a scientific software manufacturer
- Teach courses and train students
- Design of experiments (2)

Branches of computational chemistry

There are two main branches of computational chemistry: one is based on classical mechanics, and the other is based on quantum mechanics. Molecules are sufficiently small objects that, strictly speaking, the

laws of quantum mechanics must be used to describe them. However, under the right conditions, it is still sometimes useful (and much faster computationally) to approximate the molecule using classical mechanics. This approach is sometimes called the "molecular mechanics" (MM) or "force-field" method [1]. All molecular mechanics methods are empirical in the sense that the parameters in the model are obtained by fitting to known experimental data.

Quantum mechanical methods can usually be classified either as ab initio or semi-empirical. The first label, ab initio, means "from the beginning" and implies an approach which contains no empirical parameters. This category includes Hartree-Fock (HF), configuration interaction (CI), many-body perturbation theory (MBPT), coupled-cluster (CC) theory, and other approaches [2]. These methods, particularly Hartree-Fock theory, will be the focus of this lab. The second category, semi-empirical, includes methods which make serious approximations to the quantum mechanical laws and then employ a few empirical parameters to (hopefully) patch things up. These methods include the modified neglect of differential overlap (MNDO), Austin Model 1 (AM1), and many others. Density functional theory (DFT) [3] methods are quantum mechanical approaches which are hard to categorize as ab initio or semi-empirical. Some DFT methods are free from empirical parameters, while others rely heavily on calibration with experiment. The current trend in DFT research is to employ increasing numbers of empirical factors, making recent DFT techniques semi-empirical.(5)

One of the postulates of quantum mechanics is that the wave function contains all information which is known or can be known about a molecule. Hence, quantum mechanical methods provide all possible information about a system, in principle at least. In practice, theoretical chemists have to figure out how to extract the property from the wave function, and then they have to write computer programs to perform the analysis. However, it is now fairly routine to compute the following molecular properties:

Properties Obtainable From Quantum Mechanical Methods

- Geometrical structures (rotational spectra)
- Rovibrational energy levels (infrared and Raman spectra)
- Electronic energy levels (UV and visible spectra)
- Quantum Mechanics + Statistical Mechanics Thermochemistry (ΔH , ΔG , C_v , C_p), primarily gas phase.
- Potential energy surfaces (barrier heights, transition states); with a treatment of dynamics, this leads to reaction rates and mechanisms.
- Ionization potentials (photoelectron and X-ray spectra)
- Electron affinities
- Franck-Condon factors (transition probabilities, vibronic intensities)
- IR and Raman intensities
- Dipole moments
- Polarizabilities
- Electron density maps and population analyses
- Magnetic shielding tensors NMR spectra

Software packages in computational chemistry

Many self-sufficient computational chemistry software packages exist. Some include many methods covering a wide range, while others concentrate on a very specific range or even on one method. Details of most of them can be found in(4)

- Biomolecular modelling programs: proteins, nucleic acid.
- Molecular mechanics programs.
- Quantum chemistry and solid state physics software supporting several methods.
- Molecular design software
- Semi-empirical programs.
- Valence bond programs.

Scholar,

Department of Chemistry, Mahatma Jyoti Rao Phoolle University, Jaipur

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